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Motor-Cognitive Dual-Task Deficits in Individuals with Early-Mid Stage Huntington's disease

Nora E. Fritz, PhD, PT, DPT, NCS ¹	nora.fritz@wayne.edu
Katy Hamana, BSc, MCSP ²	debonok1@cardiff.ac.uk
Mark Kelson, PhD, MSc, BSc ³	kelsonmj@cf.ac.uk
Anne Rosser, PhD, MB, BChir, BA (Hons) ⁴	rosserae@cf.ac.uk
Monica Busse, PhD ²	busseme@cardiff.ac.uk
Lori Quinn, EdD, PT ^{2,5}	lq2165@tc.columbia.edu ; quinnl1@cardiff.ac.uk

1. Wayne State University, Program in Physical Therapy, Detroit, MI, USA
2. School of Health Care Sciences, Cardiff University, Cardiff, UK
3. Centre for Trials Research, Cardiff University, Cardiff, UK
4. Schools of Medicine and Biosciences, Cardiff University, Cardiff, UK
5. Department of Biobehavioral Sciences, Teachers College, Columbia University, New York, NY, USA

Corresponding Author:

Lori Quinn, EdD, PT
Teacher's College, Columbia University
525 West 120th Street, Box 199
New York, NY 10027
Phone: (212) 678-3424 Fax:
Email: lq2165@tc.columbia.edu; quinnl1@cardiff.ac.uk

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Abstract

Background. Huntington's disease (HD) results in a range of cognitive and motor impairments that progress throughout the disease stages; however, little research has evaluated specific dual-task abilities in this population, and the degree to which they may be related to functional ability.

Objectives. The purpose of this study was to a) examine simple and complex motor-cognitive dual-task performance in individuals with HD, b) determine relationships between dual-task walking ability and disease-specific measures of motor, cognitive and functional ability, and c) examine the relationship of dual-task measures to falls in individuals with HD. *Methods.* Thirty-two individuals with Huntington's disease were evaluated for simple and complex dual-task ability using the Walking While Talking Test. Demographics and disease-specific measures of motor, cognitive and functional ability were also obtained. *Results.* Individuals with HD had impairments in simple and complex dual-task ability. Simple dual-task walking was correlated to disease-specific motor scores as well as cognitive performance, but complex dual-task walking was correlated with total functional capacity, as well as a range of cognitive measures. Number of prospective falls was strongly correlated to dual-task measures. *Conclusions.* Our results suggest that individuals with HD have impairments in cognitive-motor dual-task ability that are related to disease progression and specifically functional ability. Dual-task measures appear to evaluate a unique construct in individuals with early to mid-stage HD, and may have value in improving the prediction of falls risk in this population.

Keywords. Huntington's disease, dual-task, motor, cognitive, falls

Introduction

Individuals with HD typically present with a range of motor impairments, including akinesia, bradykinesia, and incoordination[1] that progress over time and affect functional ability. Declines in cognition are a notable feature of the disease process, and people with HD often have difficulty holding, shifting[2] and dividing attention[3]. Difficulty with divided attention, or simultaneously monitoring two tasks, is particularly significant given that automaticity can change with damage to the nervous system; previously automatic movements, such as walking or balancing in standing may become attention demanding[4] and place an increased load on cognitive resources.

Impairments in simultaneous motor-cognitive tasks, i.e. dual-tasks, have been well documented in neurodegenerative disease populations, including Parkinson's disease (PD)[5], Alzheimer's disease[6] and Multiple Sclerosis[7]. In HD, prior studies have shown impairments while performing complex cognitive dual-tasks (competing cognitive tasks with a manual or vocal response)[8] and automaticity with bi-manual tapping tasks (motor-motor dual-task)[9], particularly as task difficulty increases. Guidelines to increase task complexity have not been established; while some have utilized decision-making as the added complexity[10], studies in other populations have utilized inhibitory control of speech[11] to probe executive functioning and task-switching control under dual-task conditions. Although early work demonstrated no relationship among cognitive performance and walking[12], recent work showed that gait speed during motor-cognitive dual-task walking (i.e., walking with backward counting) has been linked with United Huntington's Disease Rating Scale Total Motor Score (UHDRS-TMS) and performance on cognitive testing[13]. Individuals with greater cognitive impairment also demonstrate greater dual-task interference for complex cognitive tasks[10]. Although individuals

with HD can modify their walking speed in response to external cues[12,14], this ability declines with increasing gait impairment, and the impact of cognitive status on this relationship has not been determined.

Individuals with HD commonly experience falls[15]; in one prospective study, 21% of participants experienced 1 fall and 58% experienced at least 2 falls over the course of a year[15]. Difficulty performing dual-tasks has been associated with falls in people with PD[16] and multiple sclerosis[7]. Falls in HD have been linked with slower walking speed and poorer balance[15], but their relationship with dual-task performance has not been evaluated.

The purpose of this study was to a) examine simple and complex motor-cognitive dual-task performance in individuals with HD, b) determine relationships between dual-task walking ability and disease-specific measures of motor, cognitive and functional ability, and c) examine the relationships of dual-task measures to falls in individuals with HD. We hypothesized that individuals with HD would experience reductions in walking speed under dual-task conditions, and that impairments in dual-task walking would be linked with cognitive performance. We further hypothesized that dual-task assessment would be related to prospective falls.

Methods

Site and participant selection. This study utilized baseline data from the Exercise Rehabilitation Trial in Huntington's Disease (ExeRT-HD) trial[17] which was conducted across six HD specialist clinics in Europe: Cardiff, Birmingham, and Oxford, UK; Leiden, Netherlands; Munster, Germany; and Oslo, Norway (trial registration ISRCTN11392629). The study was approved by the Wales Research Ethics Committee 2 (reference number 13/WA/0315).

Inclusion and exclusion criteria. Participants were eligible for the study if they met the following criteria, which were set forth for the intervention trial. Inclusion criteria: 1) genetically

confirmed diagnosis of HD; 2) >18 years of age; 3) stable medication regime for four weeks prior to trial initiation, and 4) anticipated to maintain a stable regime for the course of trial.

Exclusion criteria: 1) any physical or psychiatric condition that would prohibit the participant from completing the intervention or full battery of assessments, 2) inability to independently use an exercise bike, 3) unable to understand or communicate in spoken English (UK sites), 4) currently involved in any intervention trial or within four weeks of completing one, 5) current, regular participation in a structured exercise program five times per week or more.

Recruitment. Participants were recruited to the ExeRT-HD trial between March 2014 and January 2015; 32 individuals met the inclusion criteria[17] for the study. Written informed consent was taken for all participants.

Assessors. Data collection was conducted by assessors at each site, who were specifically trained in the methodology utilized for collection of physical activity and functional assessments.

Assessments

Demographics. We collected age and gender, and measured participant height and weight. Medication was recorded at baseline and is reported elsewhere[17].

Disease-specific measures. The UHDRS-TMS and Total Functional Capacity (TFC) were obtained from clinical records. UHDRS-TMS and TFC scores were conducted by certified ratersⁱ within three months prior to the assessments.

Cognitive Measures. Cognitive function was assessed using the following cognitive tests: 1) Stroop color naming, word reading and interference tests[18], 2) Category Verbal Fluency Test (CVFT-Animals)[18], 3) Symbol Digit Modalities Test (SDMT)[18], and 4) Trail Making A and B[19]. This targeted cognitive battery has been optimized for HD[19] .

ⁱ Raters were certified by the European Huntington's Disease Motor Rater certification

Dual-task measures. We evaluated dual-task ability using the Walking While Talking Test (WWTT)[20]. During this test, a combination of motor and cognitive tasks were evaluated under simple and complex dual-task conditions. Participants were first asked to cite the alphabet sitting and the time and number of errors were recorded. The participants were then asked to walk for 20 ft out and back (40 ft total), and the time was recorded.ⁱⁱ The participant was then asked to walk the same distance while reciting the alphabet (simple). The time to complete the walk and the number of correct letters and number of errors was recorded. Lastly, the participant was asked to walk the same distance again while reciting every other letter of the alphabet (complex). The time to complete the walk and the number of correct letters and number of errors was recorded. Appendix A provides further detailed information about the task instructions. Dual-task cost (DTC) quantifies the change in performance under dual-task conditions relative to the single task condition[21]. Gait and Cognitive DTCs were calculated following the methods of Hall et al[21]. DTCs were expressed as percentages to examine Dual-Task Effect[22].

Falls Assessment. Falls were assessed prospectively from the time of baseline assessment over a three-month period. Falls were assessed using falls diaries, which were given to all participants at the end of the baseline assessment. Participants were asked to record at the end of each week if they had any falls, and if yes, to describe the circumstances and any injuries sustained.

Statistical Analyses. Statistical analyses were completed with Stata 11 (StataCorp, College Station TX) and SPSS Version 24 (IBM, Armonk NY). To examine relationships among dual-task walking and motor, cognitive and disease-specific measures and falls, Spearman

ⁱⁱ The assessment was administered over a total distance of 20m rather than 40ft in 10 participants at one site. This was noted during the second assessment of the eighth participant; the final three participants from this site (from 10 total participants) were subsequently evaluated under both 20m and 40ft conditions, and this data was used to estimate a conversion to the 12.2m distance for all participants.

correlations were used; bootstrapping analysis was performed to calculate 95% confidence intervals. Using Mann-Whitney tests, we compared performance along the disease spectrum by dividing the group at the median UHDRS-TMS. Walking velocity was calculated from timed walking speed on the baseline condition of the WWTT. Finally, we completed a sub-analysis on individuals who returned prospective falls diaries to understand if dual-task measures are related to falls in HD.

Results

Individuals performed all testing in a single day in a standardized order. Demographic information is shown in Table 1.

Dual-Task Performance. Under dual-task conditions, gait speed declined significantly from baseline in both the simple ($p=0.004$) and complex ($p=0.001$) conditions. Figure 1 shows that the majority of individuals prioritized gait with a decline in cognition, or experienced mutual interference, with declines in both gait and cognitive performance.

Relationship of Dual-Task Walking Time to Motor and Function Scores: Time to complete the WWTT-simple was moderately correlated with UHDRS-TMS, but not age, gender, or TFC (Table 2; Figure 2A). Interestingly, the WWTT-complex was not related to UHDRS-TMS, but was strongly correlated with TFC, with faster times to complete the complex walking condition linked with higher TFC scores (i.e., higher independence) (Table 2). Gait and cognitive DTC measures were not related to motor or function scores ($r<|0.22|$; $p>0.23$).

Relationship of Dual-Task Walking Time to Cognitive Performance: Slower time to complete the WWTT-simple was moderately correlated with poorer performance on the Trail Making Test, Stroop word and interference, and SDMT (Table 3; Figure 2B). Similarly, slower time to

complete the WWTT-complex was moderately correlated with poorer performance on both Trails A and Trails B, as well as poorer performance on the color, word, and interference conditions of the Stroop and the SDMT (Table 3). Gait and cognitive DTC for the simple or complex conditions were not related to cognitive measures ($r < |0.21|$; $p > 0.26$).

Dual-Task Measurement May be Particularly Useful in Individuals with UHDRS-TMS < 35 . To examine relationships of dual-task measures to cognition along the disease spectrum, we split the group by the median UHDRS-TMS score, 35, resulting in 16 individuals in each group.

Comparisons between groups are shown in Table 1.

In individuals with $TMS < 35$, timed walking and WWTT-simple were related to Trails A ($r = 0.53$; $p = 0.04$; CI (-0.004 to 0.80) and $r = 0.70$; $p = 0.003$; CI (0.29 to 0.93), respectively) and B ($r = 0.55$; $p = 0.03$; CI (-0.16 to 0.82) and $r = 0.52$; $p = 0.04$; CI (-0.003 to 0.83), respectively) performance but no other measures of cognition. Similarly, timed walking and simple dual-task walking were correlated with gender ($r = 0.63$; $p = 0.01$; CI (0.06 to 0.87) and $r = 0.50$; $p = 0.05$; CI (-0.11 to 0.84), respectively) but no other disease specific measures. Interestingly, WWTT-complex performance was strongly correlated with TFC ($r = -0.63$; $p = 0.01$; CI (-0.90 to -0.22)) as well as Trails A performance ($r = 0.54$; $p = 0.03$; CI (0.06 to 0.83)).

In individuals with $TMS \geq 35$, none of the walking measures were related to demographic or disease-specific measures or to any of the cognitive measures.

Relationship of Dual-Task Measures to Prospective Falls. Nineteen individuals completed and returned the prospective falls diary (response rate = 59%). The diaries indicated the number of falls that had occurred in the subsequent 3 months following baseline assessment. We completed a sub-analysis on these 19 subjects (mean (SD) age: 50.2(14.1); TMS: 35.6 (20.6); TFC: 8.1

(2.9); gender: 10M; 9F) to examine relationships among motor, cognitive and dual-task measures and prospective falls.

Although the number of prospective falls was not related to timed walking ($r=0.426$; $p=0.069$; CI (-0.07 to 0.74)), they were strongly correlated to WWTT-simple ($r=0.86$; $p<0.001$; CI (0.62 to 0.96)), and moderately correlated with WWTT-complex ($r=0.44$; $p=0.058$; CI (0.01 to 0.73)). This indicates that these measures of walking and dual-task walking may be useful clinical tools to predict future falls in individuals with HD.

Interestingly, when we divided the fallers by UHDRS-TMS score, the prospective number of falls ($n=10$ reporters) in individuals with $TMS<35$ was not related to the walking measures; however, in individuals with $TMS\geq 35$ ($n=9$ reporters), prospective falls were strongly correlated with both walking ($r=0.84$; $p=0.004$; CI (0.56 to 0.95) and dual-task walking ($r=0.85$; $p=0.004$; CI (0.63 to 0.95) for simple and $r=0.76$; $p=0.02$; CI (0.23 to 0.96) for complex).

Discussion

This paper is the first to report the presence of cognitive-motor dual-task deficits in people with early-mid stage HD. Our results suggest that individuals with HD have impairments in cognitive-motor dual-task ability that are related to disease progression and specifically global functional abilities. Dual-task measures appear to evaluate a unique construct in individuals with early to mid-stage HD, and dual-task measures may have value in improving the prediction of falls risk in this population.

In this study, we evaluated both simple and complex dual-task during a walking while talking task. Task complexity was increased by adding an inhibitory speech component to the “complex” dual-task condition. Previous work has shown that performing a cognitive-motor

dual-task resulted in a greater deterioration of gait speed and parameters (including stride to stride variability) in patients with HD compared to healthy controls[13]. In our cohort, the decline in gait speed with dual-task performance was comparable to individuals with PD[23]. Furthermore, cognitive-motor dual-tasks have been shown to be more impaired compared to two motor tasks completed simultaneously[13]. In people with neurologic disease, previously automatic tasks may become attention demanding[24]; thus, tasks like walking or balance in standing may require greater cognitive resources. The cognitive reserve hypothesis theorizes that innate intelligence and level of education are related to progression of disease symptoms[25] and the brain's capacity to cope with the neurodegenerative disease process[26]. Higher cognitive reserve has been associated with better cognitive performance and a significant slowing in cognitive decline in PD[27]. Figure 1 shows that most individuals with HD in our cohort experienced mutual interference, resulting in declines of both gait and cognitive performance under dual-task conditions. Importantly, many subjects prioritized gait ability; as walking becomes more cognitively demanding, individuals with HD may choose to attend to walking ability, leaving fewer cognitive resources for other tasks.

An interesting finding in this study was the differing relationship of simple and complex dual-tasks to UHDRS-TMS and TFC scores. Simple dual-task was associated with UHDRS-TMS, but not TFC while complex dual-task was strongly related to TFC but not to UHDRS-TMS. The simple dual-task, which required participants to walk at a comfortable pace while saying the alphabet, may have placed more emphasis on the motor component (walking), as reciting the alphabet may not have been particularly demanding from a resource allocation perspective. The complex nature of saying every other letter, however, clearly pushed participant's cognitive abilities, and thus is more related to the TFC score; a general measure of

function incorporating cognitive and motor abilities. The TFC is often used as an indication of overall independent functioning; thus, assessment of complex dual-tasks may aid clinicians in determining daily function of an individual and could cue necessary referrals for rehabilitation.

Dual-task function represents a unique construct that may be particularly important in a complex, neurodegenerative disease such as HD, in which cognitive and motor impairments are hallmarks of the disease from an early stage. With the ever-increasing number of pharmacologic and other clinical trials aimed at slowing disease progression, there is an urgent need for clinical end points that can readily be used in clinical settings and across disease stages. While motor evaluations, such as the UHDRS-TMS, and cognitive measures, including Trails A, may be sensitive measures of disease progression[28], dual-task may measure a unique construct that encompasses both cognitive and motor impairments from an early stage. Recent work by Vaportzis et al.[8] suggests that dual-task measures may be a better measure of cognitive processing in HD, and that impaired automaticity may be responsible for these impairments. The main site of early pathology in HD is the striatum, which may play a role in dual-information processing[8]. The basal ganglia have been shown to be active during implementation of learned motor programs[29], which may lend support to clinical observations of loss of automaticity in HD[9].

Dual-task measures may be particularly useful for identifying cognitive decline in patients in early stages of the disease. For participants with UHDRS-TMS<35, WWTT-simple were related to Trails A and B performance, while WWTT-complex performance was significantly related to both TFC and Trails A performance. In individuals with UHDRS-TMS<35, prospective falls were not related to walking measures; however, dual-task measures may be indicative of fall risk in individuals with UHDRS-TMS \geq 35. For this group, dual-task

walking measures were not related to cognitive or disease-specific measures, but prospective falls were strongly related to dual-task walking. This suggests that dual-task measures may have differential usefulness across the spectrum of motor severity. Larger sample sizes are necessary to confirm this hypothesis.

Gait speed has been shown to be sensitive to disease progression in HD[30], however its relationship to balance and falls risk in this population has not been established. In this study, ability to perform another task while walking was related to reported falls. Fall prediction in neurodegenerative diseases has proved challenging, likely due to the many impairment and environmental factors that contribute to falls. Dual-task measures incorporate motor and cognitive functioning in a unique way that challenges individuals with HD and may be useful for clinicians examining fall risk in HD.

While dual-task measures may be useful assessment tools to probe cognitive function or fall risk in HD, little is known about how individuals with HD may respond to targeted dual-task training. Specific motor-cognitive dual-task interventions have been undertaken in many neurologic populations with overall success at improving dual-task ability in walking. In one study[31], individuals with HD participated in a video-game based training program requiring participants to step to targets in response to cues on a screen, thereby incorporating both motor and cognitive components. Kloos et al. found that individuals with less severe motor impairment responded better to this intervention than those with more severe impairments[31]. This suggests that specific interventions aimed at addressing dual-task problems should be the focus of rehabilitation interventions from the early stages of HD.

While this study is the first to report the presence of dual-task impairments and their relation to falls in HD, this was a relatively small sample size and should be repeated in a larger

patient population. A more representative group of patients across the disease spectrum would be necessary to determine if cognitive-motor dual-task measures will be a sensitive marker of disease progression. Prospective falls information corroborated by carers would strengthen the findings, as maintaining fall diaries can be challenging for individuals with HD. Future work should consider the effect of task type and complexity of dual task ability. In addition, future studies are required to more fully elucidate factors contributing to falls risk in this population, including both dual-task measures and a more comprehensive assessment of balance and coordination.

Conclusions

Individuals with HD experience dual-task deficits related to disease progression and global functional ability. Dual-task measures a unique construct in HD and has the potential to improve fall prediction. Future studies should examine the utility of dual-task measures as clinical endpoints and explore interventions to improve dual-task performance in HD.

Conflict of Interest Statement.

All authors declare no conflicts of interest.

Table 1. Demographics and performance on functional and disease-specific measures in all subjects and when subdivided by UHDRS-TMS score.

	HD (n= 32)	UHDRS- TMS<35 (n=16)	UHDRS-TMS ≥35 (n=16)
Age (years)	52.0 (14.0)	45.6 (14.2)	58.4 (10.7)*
Gender (M:F)	16:16	5:11	11:5
TFC	8.4 (2.9)	9.1 (2.4)	7.8 (3.2)
UHDRS-TMS	35.8 (19.0)	20.6 (8.0)	51.1 (13.6)**
SDMT # correct	25.3 (9.9)	29.3 (9.3)	21.3 (9.2)*
Stroop # correct			
Word	60.0 (18.2)	65.8 (14.5)	54.1 (20.1)
Color	44.1 (14.6)	48.1 (14.0)	40.1 (14.4)
Interference	24.5 (8.9)	29.1 (7.5)	20.9 (8.5)*
Trail Making Test (s)			
A	69.4 (47.2)	56.2 (30.7)	82.5 (57.3)
B	143.1 (67.0)	124.2 (69.0)	164.6 (59.8)
CVFT #correct	15.1 (5.4)	17.1 (4.8)	13.1 (5.3)
WWTT			
Timed Walking (s)	11.9 (4.1)	10.5 (2.5)	13.3 (4.9)
Simple (s)	13.4 (5.6)	11.9 (3.3)	14.9 (7.0)
Complex (s)	19.5 (14.0)	17.1 (8.5)	21.9 (17.9)
Gait DTC Simple	0.13 (0.19)	0.14 (0.18)	0.12 (0.21)
Gait DTC Complex	0.61 (0.65)	0.63 (0.55)	0.59 (0.75)
Cognitive DTC Simple	-0.04 (0.46)	-0.037 (0.44)	-0.045 (0.49)
Calculated Walking Speed at Baseline (m/s)	1.13 (0.33)	1.23 (0.079)	1.03 (0.085)

All values are shown mean (SD). * Indicates that the TMS≥35 was significantly different from the TMS<35 group at p<0.05 or **p<0.01.

Total Functional Composite (TFC); United Huntington's Disease Rating Scale-Total Motor Score (UHDRS-TMS); Symbol Digit Modalities Test (SDMT); Category Verbal Fluency Test (CVFT); Walking While Talking Test (WWTT); Dual-Task Cost (DTC).

Table 2. Relationship of Walking Measures to UHDRS-TMS and TFC Scores.

		Spearman's Rho	95% Confidence Interval
Baseline Walking	UHDRS-TMS TFC	0.397* -0.281	-0.015 to 0.670 -0.594 to 0.095
Calculated Walking Speed	UHDRS-TMS TFC	-0.395* 0.281	-0.676 to -0.009 -0.087 to 0.593
WWTT-Simple	UHDRS-TMS TFC	0.374* -0.287	-0.006 to 0.661 -0.625 to 0.082
WWTT-Complex	UHDRS-TMS TFC	0.310 -0.618**	-0.057 to 0.606 -0.832 to -0.321

* $p < 0.05$; ** $p < 0.01$. Total Functional Composite (TFC); United Huntington's Disease Rating Scale-Total Motor Score (UHDRS-TMS); Walking While Talking Test (WWTT).

Table 3. Relationship of Walking Measures to Cognitive Performance.

		Spearman's Rho	95% Confidence Interval
Baseline Walking	Trails A	0.401*	-0.053 to 0.725
	Trails B	0.396*	0.038 to 0.704
	Stroop Color	-0.261	-0.623 to 0.134
	Stroop Word	-0.412*	-0.751 to 0.084
	Stroop Interference	-0.415*	-0.686 to 0.027
	SDMT	-0.447*	-0.737 to -0.024
Calculated Walking Speed	Trails A	-0.420*	-0.665 to -0.014
	Trails B	-0.396*	-0.692 to -0.026
	Stroop Color	0.261	-0.193 to 0.619
	Stroop Word	0.377*	-0.097 to 0.736
	Stroop Interference	0.396*	-0.122 to 0.734
	SDMT	0.447*	-0.009 to 0.763
WWTT-Simple	Trails A	0.520*	0.050 to 0.750
	Trails B	0.418*	0.007 to 0.735
	Stroop Color	-0.337	-0.665 to 0.076
	Stroop Word	-0.419*	-0.694 to -0.013
	Stroop Interference	-0.510**	-0.760 to -0.124
	SDMT	-0.432*	-0.728 to 0.007
WWTT-Complex	Trails A	0.527**	0.158 to 0.745
	Trails B	0.510**	0.131 to 0.787
	Stroop Color	-0.372*	-0.694 to 0.106
	Stroop Word	-0.353*	-0.694 to 0.093
	Stroop Interference	-0.377*	-0.648 to 0.057
	SDMT	-0.499**	-0.730 to -0.122

* p<0.05; **p<0.01. Symbol Digit Modalities Test (SDMT); Walking While Talking Test (WWTT).

References

- [1] J.P.P. van Vugt, K.K.E. Piet, L.J. Vink, S. Siesling, A.H. Zwinderman, H.A.M. Middelkoop, R.A.C. Roos, Objective assessment of motor slowness in Huntington's disease: clinical correlates and 2-year follow-up., *Mov. Disord.* 19 (2004) 285–97. doi:10.1002/mds.10718.
- [2] N. Georgiou, J.L. Bradshaw, J.G. Phillips, E. Chiu, Effect of directed attention in Huntington's disease., *J. Clin. Exp. Neuropsychol.* 19 (1997) 367–77. doi:10.1080/01688639708403865.
- [3] R. Sprengelmeyer, A.G. Canavan, H.W. Lange, V. Homberg, Associative learning in degenerative neostriatal disorders: contrasts in explicit and implicit remembering between Parkinson's and Huntington's diseases, *Mov Disord.* 10 (1995) 51–65. doi:10.1002/mds.870100110.
- [4] G. Yogev-Seligmann, N. Giladi, M. Brozgov, J.M. Hausdorff, A training program to improve gait while dual tasking in patients with Parkinson's disease: a pilot study, *Arch Phys Med Rehabil.* 93 (2012) 176–181. doi:10.1016/j.apmr.2011.06.005.
- [5] S. O'Shea, M.E. Morris, R. Iansek, Dual task interference during gait in people with Parkinson disease effects of motor versus cognitive secondary tasks., *Phys. Ther.* 82 (2002) 888–897. papers://5a68cd75-9e27-4626-8d94-057f1df96060/Paper/p594\npapers://5a68cd75-9e27-4626-8d94-057f1df96060/Paper/p405.
- [6] R. Camicioli, D. Howieson, S. Lehman, J. Kaye, Talking while walking: the effect of a dual task in aging and Alzheimer's disease., *Neurology.* 48 (1997) 955–958. doi:10.1212/WNL.48.4.955.
- [7] D.A. Wajda, R.W. Motl, J.J. Sosnoff, Dual task cost of walking is related to fall risk in persons with multiple sclerosis, *J. Neurol. Sci.* 335 (2013) 160–163. doi:10.1016/j.jns.2013.09.021.
- [8] E. Vaportzis, N. Georgiou-Karistianis, A. Churchyard, J.C. Stout, Effects of task difficulty during dual-task circle tracing in Huntington's disease., *J. Neurol.* 262 (2015) 268–76. doi:10.1007/s00415-014-7563-9.
- [9] J.C. Thompson, E. Poliakoff, A.C. Sollom, E. Howard, D. Craufurd, J.S. Snowden, Automaticity and attention in Huntington's disease: when two hands are not better than one., *Neuropsychologia.* 48 (2010) 171–8. doi:10.1016/j.neuropsychologia.2009.09.002.
- [10] E. Vaportzis, N. Georgiou-Karistianis, A. Churchyard, J. Stout, Dual Task Performance in Huntington's Disease: A Comparison of Choice Reaction Time Tasks, *Neuropsychology.* 29 (2015) 703–712. doi:10.1037/neu0000172.
- [11] J. Verghese, H. Buschke, L. Viola, M. Katz, C. Hall, G. Kuslansky, R. Lipton, Validity of divided attention tasks in predicting falls in older individuals: A preliminary study, *J. Am. Geriatr. Soc.* 50 (2002) 1572–1576. doi:10.1046/j.1532-5415.2002.50415.x.

- [12] A.J. Churchyard, M.E. Morris, N. Georgiou, E. Chiu, R. Cooper, R. Iansek, Gait dysfunction in Huntington's disease: parkinsonism and a disorder of timing. Implications for movement rehabilitation, *Adv Neurol.* 87 (2001) 375–385.
- [13] A. Delval, P. Krystkowiak, M. Delliaux, K. Dujardin, J.L. Blatt, A. Destee, P. Derambure, L. Defebvre, Role of attentional resources on gait performance in Huntington's disease, *Mov Disord.* 23 (2008) 684–689. doi:10.1002/mds.21896.
- [14] A. Delval, P. Krystkowiak, M. Delliaux, J.L. Blatt, P. Derambure, A. Destée, L. Defebvre, Effect of external cueing on gait in Huntington's disease., *Mov Disord.* (2008). http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18512747.
- [15] M.E. Busse, C.M. Wiles, A.E. Rosser, Mobility and falls in people with Huntington's disease., *J Neurol Neurosurg Psychiatry.* 80 (2009) 88–90. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=19091714.
- [16] J. V Jacobs, J.G. Nutt, P. Carlson-Kuhta, R. Allen, F.B. Horak, Dual tasking during postural stepping responses increases falls but not freezing in people with Parkinson's disease, *Park. Relat. Disord.* 20 (2014) 779–781. doi:10.1016/j.parkreldis.2014.04.001.
- [17] Quinn L, Hamana K, Kelson M, Dawes H, Collett J, Townson J, Roos R, van der Plas AA, Reilmann R, Frich J, Rosser A, Multimodal Exercise Improves Fitness and Motor Function in People with Huntington Disease: Results from a Randomized, Feasibility Trial, *Neurotherapeutics.* 13 (2016) 248–249.
- [18] H.S. Group, Unified Huntington's Disease Rating Scale: reliability and consistency, *Mov Disord.* 11 (1996) 136–142.
- [19] J.C. Stout, S. Queller, K.N. Baker, S. Cowlshaw, C. Sampaio, C. Fitzner-Attas, B. Borowsky, HD-CAB: A cognitive assessment battery for clinical trials in Huntington's disease(1,2,3.), *Mov Disord.* 29 (2014) 1281–1288. doi:10.1002/mds.25964.
- [20] J. Verghese, H. Buschke, L. Viola, M. Katz, C. Hall, G. Kuslansky, R. Lipton, Validity of divided attention tasks in predicting falls in older individuals: a preliminary study., *J. Am. Geriatr. Soc.* 50 (2002) 1572–6. <http://www.ncbi.nlm.nih.gov/pubmed/12383157> (accessed November 25, 2015).
- [21] C.D. Hall, K. V Echt, S.L. Wolf, W. a Rogers, Cognitive and motor mechanisms underlying older adults' ability to divide attention while walking., *Phys. Ther.* 91 (2011) 1039–1050. doi:10.2522/ptj.20100114.
- [22] P. Plummer, G. Eskes, Measuring treatment effects on dual-task performance: a framework for research and clinical practice., *Front. Hum. Neurosci.* 9 (2015) 225. doi:10.3389/fnhum.2015.00225.
- [23] P. Ginis, A. Nieuwboer, M. Dorfman, A. Ferrari, E. Gazit, C.G. Canning, L. Rocchi, L. Chiari, J.M. Hausdorff, A. Mirelman, Feasibility and effects of home-based smartphone-

- delivered automated feedback training for gait in people with Parkinson's disease: A pilot randomized controlled trial, *Parkinsonism Relat. Disord.* (2015). doi:10.1016/j.parkreldis.2015.11.004.
- [24] G. Yogev-Seligmann, J.M. Hausdorff, N. Giladi, The role of executive function and attention in gait., *Mov. Disord.* 23 (2008) 329–42; quiz 472. doi:10.1002/mds.21720.
 - [25] A. Bonner-Jackson, J.D. Long, H. Westervelt, G. Tremont, E. Aylward, J.S. Paulsen, Cognitive reserve and brain reserve in prodromal Huntington's disease., *J. Int. Neuropsychol. Soc.* 19 (2013) 739–50. doi:10.1017/S1355617713000507.
 - [26] K.L. Siedlecki, Y. Stern, A. Reuben, R.L. Sacco, M.S. V Elkind, C.B. Wright, Construct validity of cognitive reserve in a multiethnic cohort: The Northern Manhattan Study., *J. Int. Neuropsychol. Soc.* 15 (2009) 558–69. doi:10.1017/S1355617709090857.
 - [27] J. V Hindle, A. Martyr, L. Clare, Cognitive reserve in Parkinson's disease: a systematic review and meta-analysis., *Parkinsonism Relat. Disord.* 20 (2014) 1–7. doi:10.1016/j.parkreldis.2013.08.010.
 - [28] S. Franciosi, Y. Shim, M. Lau, M.R. Hayden, B.R. Leavitt, A systematic review and meta-analysis of clinical variables used in Huntington disease research., *Mov. Disord.* 28 (2013) 1987–94. doi:10.1002/mds.25663.
 - [29] C. Marsden, The mysterious motor functions of the basal ganglia: The Robert Wartenburg Lecture, *Neurology.* 32 (1982) 514–539.
 - [30] L. Quinn, H. Khalil, H. Dawes, N.E. Fritz, D. Kegelmeyer, A.D. Kloos, J.W. Gillard, M. Busse, Reliability and minimal detectable change of physical performance measures in individuals with pre-manifest and manifest Huntington disease, *Phys Ther.* 93 (2013) 942–956. doi:10.2522/ptj.20130032.
 - [31] A.D. Kloos, N.E. Fritz, S.K. Kostyk, G.S. Young, D.A. Kegelmeyer, Video game play (Dance Dance Revolution) as a potential exercise therapy in Huntington's disease: a controlled clinical trial, *Clin Rehabil.* 27 (2013) 972–982. doi:10.1177/0269215513487235.

Figure 1. An examination of the dual-task effects of the cognitive and gait conditions[22] on the WWTT-simple reveals that the majority of individuals with HD in this cohort either experienced mutual interference, where both gait and cognitive performance declined under dual-task conditions, or prioritized gait, such that gait speed increased but cognitive performance decreased under dual-task conditions. The dual-task effect is the calculated percent difference between performance in the single task and performance in the dual-task. This was calculated for both the gait and cognitive conditions and this is shown on the y- and x-axis, respectively.

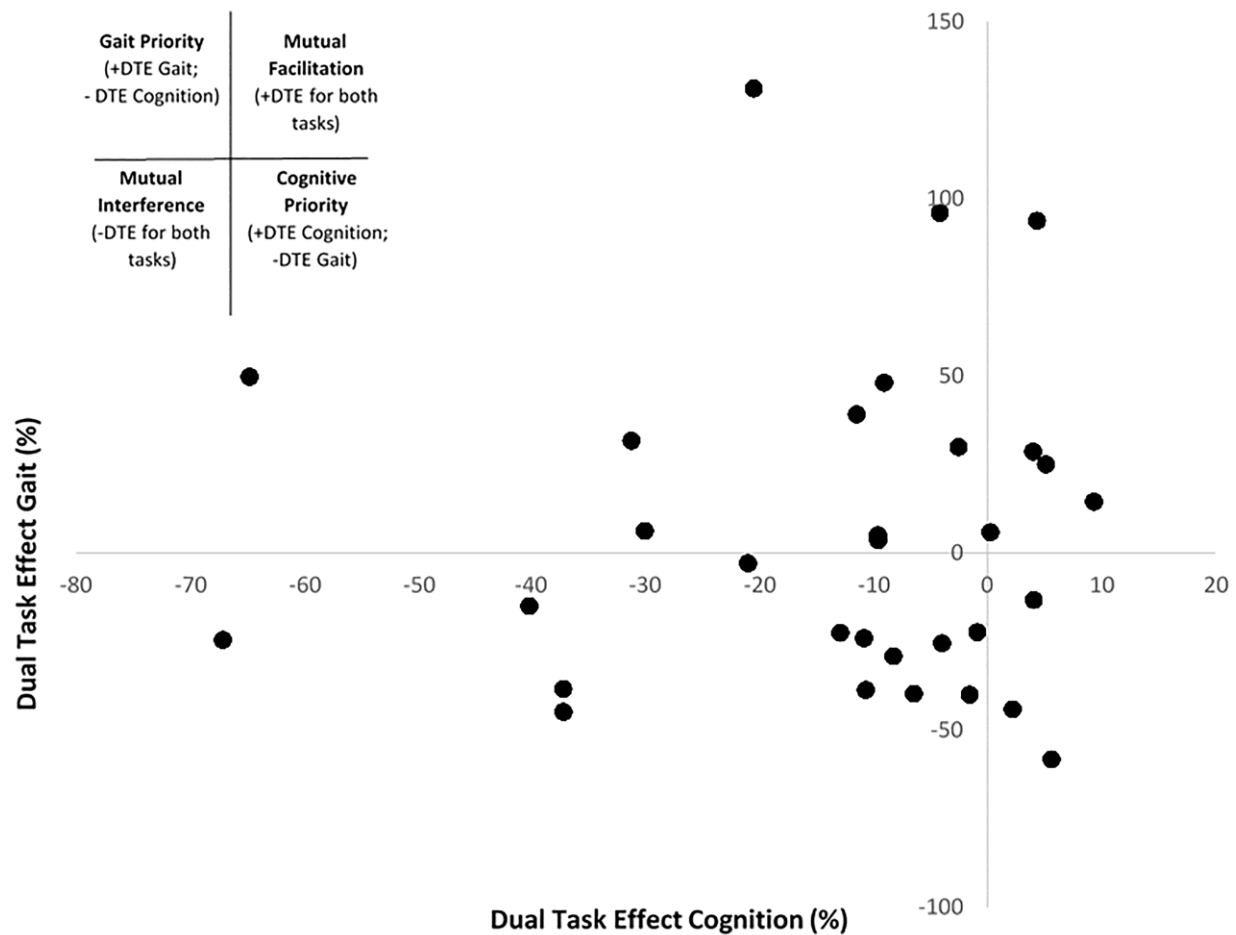
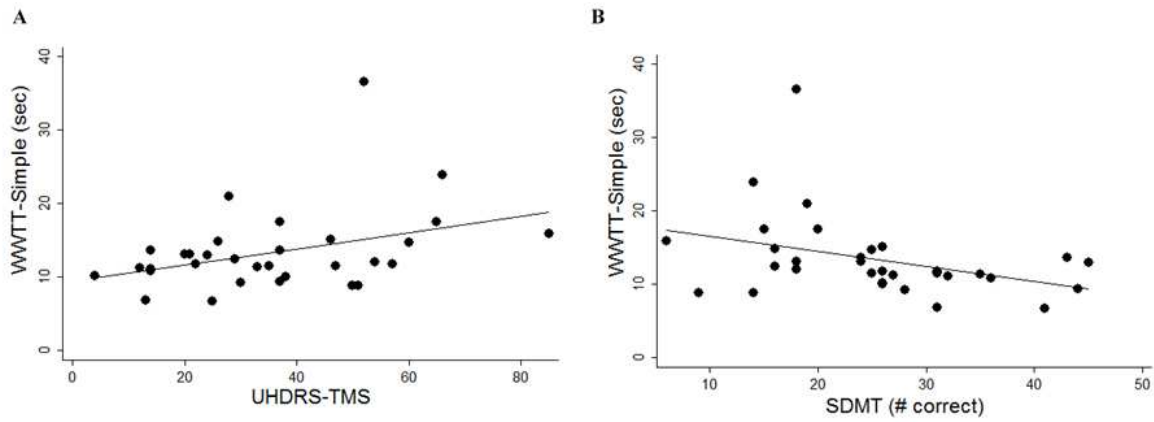


Figure 2. WWTT-Simple is associated with A) UHDRS-TMS ($r=0.3737$; $p=0.0351$) and B) SDMT performance ($r=-0.4322$; $p=0.0152$), suggesting that that dual-task assessment measures a unique construct that is highly related to both functional and cognitive performance in individuals with HD.



Appendix A: Standard Operating Procedures for Administration of Dual-Task Testing

Timed Gait

Task: Participant should be instructed to walk 20ft (6.1m) to the marker turn around and return back to the starting point (40 ft in total) at their own normal walking pace.

Instructions: “I want you to walk at your normal pace around this cone and turn and come back to here. Ready? Go.”

Scoring: Score the time to complete test to nearest 10th of a second

Cognitive seated task

Task: Time how long it takes the participant to complete reciting the alphabet from A-Z while seated.

Instructions: “I want you to recite the alphabet from A-Z, pronouncing each letter. Ready? GO”

Scoring: Follow the tick boxes in the data collection form as they recite the letters out loud, marking any incorrect with a ‘X’. Record number correct, number of errors and time to complete the task.

Walking while talking - simple

Task: Instruct the participant to walk 20ft (6.1m) to the marker turn around and return back to the starting point (40 ft in total) at their own normal walking pace, this time reciting the alphabet as they are walking.

Instructions: “I want you to walk at your normal pace around this cone and turn and come back to here. While you are doing this, recite the alphabet starting with the letter A, pronouncing each letter. Ready? GO”

Scoring: Record if any mistakes are made and the time taken to complete the distance.

Walking while talking - complex:

Task: Instruct the participant to walk 20ft (6.1m) to the marker turn around and return back to the starting point (40 ft in total) at their own normal walking pace, this time reciting every other letter of the alphabet as they are walking, starting with ‘A’.

Instructions: “I want you to walk at your normal pace around this cone and turn and come back to here. While you are doing this, recite EVERY OTHER letter of the alphabet starting with the letter A, pronouncing each letter. Ready? GO”

Scoring: Record if any mistakes are made and the time taken to complete the distance.